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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,869	08/06/2003	Gary Michael Kayajanian		7616

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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/634,869	KAYAJANIAN, GARY MICHAEL	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Informalities

1. Claims 1-19 are currently pending. Claim 20 is withdrawn from further consideration as being drawn to non-elected material.

Election/Restrictions

2. Applicant's election with traverse of Group I, Claims 1-19 in the reply filed on January 4, 2006 is acknowledged. The traversal is on the ground(s) that some heart diseases are the equivalent of "cancers of the heart" as thus should be examined with the prevention of cancer claims in the elected group. This is not found persuasive because of the reasons set forth in the Restriction Requirement dated December 12, 2005. Heart disease and cancer have different etiologies and treatments. The fact that the Applicant considers some heart diseases to be the equivalent of "cancers of the heart" is not a persuasive argument for examining the claims together.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a

separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

4. Applicant is reminded of the proper content of an abstract of the disclosure:

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:

(1) if a machine or apparatus, its organization and operation;

(2) if an article, its method of making;

(3) if a chemical compound, its identity and use;

(4) if a mixture, its ingredients;

(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

5. The abstract of the disclosure is objected to because it fails to describe the invention being claimed. The Abstract only gives a brief summary of related case studies but does not describe the claimed invention nor does it provide the steps for practicing the claimed methods.

Claim Rejections - 35 USC § 112 – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-19 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to methods of reducing total cancer and heart disease related deaths by increasing and maintaining the level of arsenic in drinking water to between 25 and 75 μg/L. However, Applicant has only provided anecdotal evidence that this method will work. In fact, no

experiments were carried out and no examples were provided that show the Applicant had possession of the claimed invention at the time the application was filed.

7. Claims 1-12 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims recite the limitation "arsenic level" but it is not clear how the level of arsenic will be increased and/or maintained and what form of arsenic will be used (e.g. As_2O_3, As_4O_6, etc.) to increase the arsenic level in drinking water. In addition, Applicant has not indicated if this method will be used to increase the level of arsenic in drinking water worldwide or in a limited area. For example, the limitation "drinking water" could be interpreted as an 8 oz. glass of water. It is not clear how one would practice the claimed invention since no guidance is provided in how one would increase the level of arsenic in an 8 oz glass of water (form of arsenic, amount of arsenic, etc.).

8. Claims 13-19 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims recite the limitation

"maintaining" but it is not clear how the level of arsenic will be maintained and for how long it will be maintained. In addition, it is not clear how Applicant intends to practice the claimed invention of maintaining arsenic levels at 25 to 75 μg/L when current EPA standards set a limit of 10 μg/L arsenic in drinking water.

9. Claims 1-7 and 12-19 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite the limitation "25-<75 μg/L" but the meaning of the arrangement of the symbolic notations is not clear. For instance, it is not clear if applicant means 25 to 75 or 25 less than 75. Thus, the range intended by the symbolic notation is indefinite.

Claim Rejections - 35 USC § 112 - Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-19 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of arsenic hexoside (As_4O_6) in tablet form to treat various cancers (as disclosed in the Bae patent), does not reasonably provide enablement for methods of reducing cancer and heart disease mortality by increasing and maintaining the arsenic level in drinking water to between 25 and 75 μg/L. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In the instant case, Applicant provides no evidence, aside from citing three data sets, that increasing levels of arsenic in drinking water will lead to decreased cancer and heart disease mortalities. In fact, as Applicant has noted, EPA regulators and scientists have shown that arsenic is carcinogenic at multiple tissue sites. In addition, the EPA recently set forth a new regulation of a maximum of 10 μg/L total arsenic in drinking water, thereby lowering the previous maximum from 50 to 10 ppb. The EPA estimates that reducing arsenic from 50 to 10 μg/L will prevent ~19-31 cases of bladder cancer and ~5-8 deaths due to bladder cancer per year. The EPA further estimates that reducing arsenic from 50 to 10 μg/L will prevent ~19-25 cases of lung cancer and ~16-22 deaths due to lung cancer per year (*Technical Fact Sheet: Final Rule for Arsenic in Drinking Water*, published January 2001, accessed from www.epa.gov on April 17, 2006). In addition, studies have linked long-term exposure to arsenic in drinking water to cancer of the bladder, lungs, skin, kidney, nasal passages, liver, and prostate. Non-cancer effects of ingesting arsenic include cardiovascular, pulmonary, immunological, neurological, and endocrine (e.g., diabetes) effects. Short-term exposure to high doses of arsenic can cause other adverse health effects, but such effects were unlikely to occur from U.S. public water supplies that were in compliance with the previous arsenic standard of 50 ppb. EPA set the previous standard of 50 ppb in 1975, based on a Public Health Service standard originally established in 1942. A March 1999 report by the National Academy of Sciences concluded that the current standard *does not*

achieve EPA's goal of protecting public health and should be lowered as soon as possible.

The following is taken directly from the *EPA Fact Sheet on Arsenic in Drinking Water* (published January 2001, accessed from www.epa.gov on April 17, 2006):

> On June 22, 2000, EPA proposed a new drinking water standard of 5 ppb for arsenic and requested comment on options of 3 ppb, 10 ppb and 20 ppb. EPA evaluated over 6,500 pages of comments from 1,100 commenters. EPA set the new arsenic standard for drinking water at 10 ppb to protect consumers against the effects of long-term, chronic exposure to arsenic in drinking water. EPA used its discretionary authority under the 1996 Amendments to the Safe Drinking Water Act to set the standard at a level that "maximizes health risk reduction benefits at a cost that is justified by the benefits." The new standard will apply to all 54,000 community water systems. A community water system is a system that serves 15 locations or 25 residents year-round, including most cities and towns, apartments, and mobile home parks with their own water supplies. EPA estimates that roughly five percent, or 3,000, of community water systems, serving 11 million people, will have to take corrective action to lower the current levels of arsenic in their drinking water. The new standard also applies to 20,000 water systems that serve at least 25 of the same people more than six months of the year, such as schools, churches, nursing homes, and factories. EPA estimates that five percent, or 1,100, of these water systems, serving approximately 2 million people, will need to take measures to meet the new arsenic standard. Of all of the affected systems, 97 percent are small systems that serve fewer than 10,000 people each.

Given the above regulation which set an upper limit of 10 μg/L total arsenic in drinking water and the profound evidence that arsenic is linked to numerous cancers and other health problems, the present invention is not enabled for claims to reduce cancer and heart disease related deaths by increasing the arsenic in drinking water to between 2.5 and 7.5x the current standard. This is especially true given that the previous standard

of 50 μg/L was reduced to the current level of 10 μg/L because of the increased risk of cancer and other health problems.

Thus, undue experimentation would be required in order to practice the claimed invention of reducing cancer and heart disease related deaths by increasing the level of arsenic in drinking water.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicted on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability or the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount of *prima facie* case is discussed below.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth below:

1. The quantity of experimentation necessary

The skilled artisan would expect a method of reducing cancer and heart disease mortality to be the result of the interactions of multiple biological pathways and therefore, highly unpredictable, absent a clear understanding of the structural and biochemical basis for the absolute reduction in cancer and heart disease mortality. The instant specification sets forth no such understanding or any criteria for extrapolating beyond those methods actually demonstrated.

The burden of enabling the prevention or reduction of cancer and heart disease mortality (i.e. the need for additional testing) would be greater than that of enabling a treatment of a specific cancer or form of heart disease. In the instant case, the specification does not provide guidance as to how one skilled in the art would go about reducing cancer and heart disease mortality or how a human could be prevented from developing cancer or heart disease by simply increasing the level of arsenic in drinking water. Further, there is no guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed method of reducing cancer or heart disease mortality in a human. Specifically, it is highly unlikely, and the Office would require experimental evidence to claims such as those of Claims 1-19, which claim to reduce total cancer mortality in men and women by the simple increase of arsenic in drinking water, for example.

2. The amount of direction or guidance provided

The specification provides no direction for ascertaining how to absolutely reduce total cancer and heart disease mortality and the applicant has not demonstrated that the method of increasing the level of arsenic in drinking water, for example, can reasonably be expected, *a priori*, to exhibit the requisite reduction in total cancer or heart disease mortality. Further, Applicant has provided no guidance on how increasing the level of arsenic in drinking could be used to absolutely reduce total cancer or heart disease mortality.

3. Presence or absence of working samples

There are no working examples demonstrating that increasing the level of arsenic in drinking water to between 25 and 75 μg/L will lead to a reduction in total cancer or heart diseases related deaths. Only anecdotal evidence in the form of data sets is provided but their interpretation is subjective and not evidence that the claimed methods will result in a decrease in cancer and/or heart disease related deaths. Further, the referenced data sets only compare total cancer related deaths, not cancer deaths from specific types of cancer. Thus, it is not clear from the Specification if one particular type of cancer was affected more than the others and led to biased results and interpretation of those results.

4. The nature of the invention

The claimed invention relates to the absolute reduction in total cancer and heart disease related deaths by increasing the level of arsenic in drinking water to a value 2.5 to 7.5x the current EPA standard of 10 μg/L.

5. State of the prior art

Applicant has interpreted three data sets to provide evidence that arsenic levels in drinking water can have an effect on cancer and heart disease related deaths. However, no scientific studies have been carried out to determine the effect of arsenic on cancer and heart disease related deaths. In fact, the prior art demonstrates that arsenic is a carcinogen at high doses. In addition, arsenic-containing compounds vary in toxicity to mammals according to valence state, form (inorganic or organic), physical state (gas, solution, or powder) and factors such as solubility, particle size, rates of absorption and elimination, and presence of impurities. The claims do not state what form, valence state, physical state, etc. of arsenic will be used in the present method. The prior art is clear that chronic arsenic exposure causes various cancers and other health issues. There is no evidence provided in the Specification to the contrary aside from the aforementioned anecdotal evidence and the Applicant's interpretation of three separate data sets.

6. Relative skill of those in the art

The relative skill of those in the art is generally that of a Ph.D. or M.D.

7. Predictability of the art

In the instant case, Claims 1-19 are drawn to methods of reducing total cancer and heart disease related morbidity and mortality by increasing the level of arsenic in drinking water to 2.5 to 7.5x the current EPA standard. The Specification provides an interpretation of three epidemiology data sets that the Applicant asserts provides support for the current claims. However, there are no working examples or referenced

scientific studies that provide support for the claimed invention. In fact, the prior art teaches away from the current methods. Arsenic is a known carcinogen as is evidenced by references cited by the Applicant. Applicant admits that lower and higher levels of arsenic than those claimed are harmful to humans but provides no evidence that the current levels are safe and will result in the intended result (i.e. reduction in cancer and heart disease related deaths). The anecdotal evidence of the data sets cannot provide adequate support for the claimed invention since only arsenic levels and cancer mortality were compared. There is no evidence in the data sets that arsenic exposure was directly related to a decrease in cancer death. Further, Applicant only compared total cancer deaths to arsenic levels. However, the claimed method is drawn to different types of cancers. If one type of cancer death was reduced more than others this would lead to a biased interpretation of the data sets. The nature of the invention is complex, being directed to biological and physiological processes and the manipulation of those processes to reduce cancer and heart disease mortality in humans by increasing the level of arsenic in drinking water. The state of the prior art is silent with respect to whether or not arsenic is effective in eliciting the claimed result. In fact, the prior art states that chronic exposure to arsenic causes cancer and other health problems. Further, the EPA recently lowered the maximum containment level of arsenic in drinking water from 50 to 10 ppb. Whether or not a particular biological molecule will have an effect in reducing cancer or heart disease mortality in humans is unpredictable, in that it requires empirical screening over a long period of time. In view of all of these factors and the lack of description in the disclosure regarding the use of the present

compounds in eliciting a reduction in total cancer or heart disease mortality in humans, undue experimentation would be required of the skilled artisan to practice the claimed invention.

Given the above, it is clear that the art to which the instant invention relates involves a relatively high degree of unpredictability.

8. Breadth of the Claims

The Claims are drawn to the total reduction in cancer and/or heart disease related deaths by increasing and maintaining the level of arsenic in drinking water.

Thus, the specification fails to enable one of ordinary skill in the art to practice and use the methods of Claims 1-19.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-11 and 13-19 rejected under 35 U.S.C. 103(a) as being unpatentable over Bau et al. (U.S. Patent No. 6,309,672; Issued Oct. 30, 2001).

Bau et al. teach that arsenic hexoxide (As_4O_6) has potent anticancer activity when administered to humans diagnosed with cancer of the uterus, lung, maxillary sinus, kidney, or urinary bladder (see especially Abstract and Example 11). Patients

were administered 0.053 g As_4O_6 in tablet form three times a day (total As_4O_6 was 160 mg per day) (see Column 15, Lines 51-66). The reference does not teach increasing the arsenic in drinking water to 25-75 μg/L in a method to reduce total cancer morbidity and mortality in men and women.

The instant claims differ from the reference in that they teach a method of reducing total cancer morbidity and mortality in men and women by increasing the arsenic level in drinking water to 25-75 μg/L (If the average person drinks 64 oz. of water per day, this would equate to an intake of between 1.6 and 4.8 mg arsenic per day).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to chronically administer arsenic at a lower dose than that taught by the reference in order to decrease the incidence (e.g. total cancer morbidity and mortality) of cancer in patients. One would be motivated to do so given that Bau et al. teach that their invention is an effective anticancer drug (see especially Column 18, Lines 17-20) at doses of approximately 0.160 g/day.

Examiner reminds Applicant that the obviousness rejection as outlined above only pertains to the treatment of cancer by administering a glass of water containing 25-75 μg/L arsenic. Increasing the level of arsenic in water supplies is not enabled by the disclosure as discussed in the rejection of Claims 1-19 under 35 U.S.C 112 above.

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James D. Anderson
Examiner
Art Unit 1614

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